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DOCKET NO.: ISIS-4502
Application No.: 08/078,768
Office Action Dated: September 15, 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Richard H. Tullis **Confirmation No.:** 9155

Serial No.: 08/078,768 **Group Art Unit:** 1631

Filing Date: June 16, 1993 **Examiner:** James Martinell

For: Oligonucleotide Therapeutic Agent And Methods Of Making Same

EXPRESS MAIL LABEL NO: EL 998517927 US
DATE OF DEPOSIT: October 18, 2004

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

PETITION UNDER 37 C.F.R. § 1.181

In an Office Communication dated **September 15, 2004**, the substitute Appeal Brief filed July 8, 2004 was deemed noncompliant by the Examiner. Appellant believes this petition to be properly filed under 37 C.F.R. § 1.181 as a matter outside the scope of petitions under 37 C.F.R. § 41.3. Appellant hereby petitions the Director to reconsider the Examiner's determination of non-compliance in view of the following remarks.

Statement of the facts

Appellant submitted a first Appeal Brief on April 15, 2004 to appeal the Examiner's position that claims directed to methods of selectively inhibiting the expression of a target protein in a cell producing messenger ribonucleic acids encoding the target protein are not enabled. Appellant's claims require hybridization of an oligonucleotide having a base sequence substantially complementary to a subsequence of the messenger ribonucleic acid encoding the target sequence. An example of a practical application of Appellant's claims is antisense technology. The Examiner has steadfastly held to his position that the claims of the present application do not satisfy the enablement requirement of the first paragraph of 35 U.S.C. § 112. Among the reasons the Examiner has provided for the alleged lack of enablement of the claims by the present specification is his position that the application does not enable one to make and use the invention as the claimed methods have not been demonstrated to work *in vivo*. Appellant's response to such an allegation has been to show

that success in the field of antisense technology according to the principles of Appellant's invention has been achieved, thereby ratifying the views of long-time proponents of antisense technology and converting many critics to the view that antisense works *in vivo* as taught by the present specification. The Examiner countered that no successful *in vivo* antisense trials linked to the methodology of the present application had been cited on the record. (Office Action mailed June 17, 2003 at page 21.)

Appellant answered the Examiner's allegation in his Appeal Brief submitted April 15, 2004 by citing to clinical trials of antisense therapies to definitively establish that antisense technology works *in vivo* in accordance with the principles set forth in the present application. For example, Appellant drew the Examiner's attention to the clinical successes achieved with the antisense drugs fomivirsen (Vitravene™) and GENASENSE™, noting that fomivirsen was approved by the Food and Drug Administration for the treatment of cytomegaloviral-induced retinitis in 1998 and that the Orange Book listing for fomivirsen identifies U.S. Patent Nos. 4,689,320, 5,264,423, 5,276,019, 5,442,049, and 5,595,978 as relating to that drug. (Appeal Brief submitted April 15, 2004 at page 16.)

The Examiner subsequently issued a Notice of Non-compliant Brief on June 8, 2004, indicating that, because the patents and Orange Book listing had not been made of record prior to the filing of the Appeal Brief, their citation in the appeal brief was improper.

Applicants obligingly submitted a substitute Appeal Brief on July 8, 2004 which deleted reference to the patent numbers at issue and to the Orange Book. The substitute Brief, however, retained reference to the **existence** of patents covering fomivirsen.

The Examiner has ruled the substitute Appeal Brief filed July 8, 2004 to be defective, maintaining that it refers to patents that are not of record. The Examiner has admitted, however, that the patents are not cited directly. Rather, they are alluded to by way of reference to the electronic Orange Book promulgated by the U.S. Food and Drug Administration. Nonetheless, the Examiner requires removal of any reference to patents related to fomivirsen. (Office Communication dated September 15, 2004 at page 2.)

Relief requested

The substitute Appeal Brief of July 8, 2004 retained reference to the existence of patents covering fomivirsen for the purpose of apprising the Board of Patent Appeals and Interferences of the **existence** of the patents rather than for their **content**. Appellant respectfully submits that reference to the fact that patents relating to fomivirsen have issued does not constitute new evidence not previously made of record requiring compliance with 37 C.F.R. § 41.33. Accordingly, Appellant believes the reference to the fact that patents related to fomivirsen have issued in the substitute Appeal Brief of July 8, 2004 to be entirely proper.

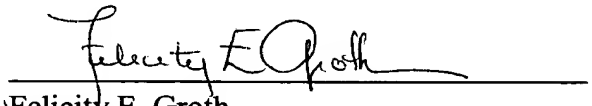
As the application will be determined to have been abandoned if the Examiner's requirements are not met by the Appellant, a second substitute Appeal Brief has been submitted with the language at issue deleted. At the same time, however, this petition under 37 C.F.R. § 1.181 is being filed to challenge the Examiner's holding of noncompliance. If

the petition is granted, it is expected that the Board will act upon the Appeal Brief of July 8, 2004.

If the Director believes a telephone conference would expedite resolution of the issue for which reconsideration is sought, the undersigned may be contacted at 215-568-3100.

Respectfully submitted,

Date: October 18, 2004



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